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EXAMINER: FOX, D

ART UNIT	PAPER NUMBER
1803	5

DATE MAILED: 04/28/95

JOSEPH T EISELE
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NEW YORK NY 10017

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☑ Responsive to preliminary communication filed on 8/2/94, 3/2/95, 2/14/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~_____~~ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☑ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1-4 and 7-26 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☑ Claims 5-6 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-4 and 7-26 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☑ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☑ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☑ been filed in parent application, serial no. 07/628,246 filed on 12/17/90.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 2/93)

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1803.

The application should be reviewed for errors. Errors appear, for example, in claim 9, line 8, where the hyphen should be deleted from the middle of "pyrophos-phorylase"; and in claim 23, line 1, where "a" should be capitalized.

A copy of the Burrell declaration filed 25 March 1993 in parent application Serial No. 07/991,451, demonstrating the function of the adenine diphosphoglucose pyrophosphorylase (ADPGPP) gene in transgenic potato plants, is requested for file completeness.

Claims 1, 10-12 and 17-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5,387,756. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would have been obvious to one of ordinary skill in the art to utilize the transgenic plant transformed with a plasmid comprising the starch metabolism ADPGPP gene claimed in the patent to obtain the constructs and transgenic plants comprising starch metabolism genes as claimed in the instant application.

Claims 1, 2, 9, 13, and 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is indefinite in its recitation of "suitable", as the purpose of the promoter is not stated, so that it is unclear what would constitute a "suitable" promoter. Claims 2, 9, 13, and 20 are indefinite in their recitation of "deoxynucleic" as it is unclear what Applicants intend. Amendment of the claims to recite --deoxyribonucleic-- would obviate this rejection.

Claims 21-26 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 21-26, which recite the coding of more than one enzyme by a single coding sequence, fail to further limit the claims from which they depend, which are drawn to a single coding sequence which encodes a single enzyme. Amending claim 2 to recite --(b) a deoxyribonucleic acid fragment comprising a coding sequence which encodes for an enzyme--, and amending claim 22 to replace "coding sequence" with --fragment--, would obviate this rejection for claim 22. Similar amendments are suggested for the other claims from which the other claims included in this rejection depend.

Claims 1-4, 7-19 and 21-26 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a process for the introduction of a gene encoding either phosphofructokinase or adenine diphosphoglucose pyrophosphorylase into the genome of a plant cell. See M.P.E.P.

§§ 706.03(n) and 706.03(z). The specification only demonstrates the utilization of a gene encoding the glycolytic enzyme phosphofructokinase for plant transformation. In addition, the Burrell declaration submitted 25 March 1993 in parent application Serial No. 07/991,451 demonstrates the utilization of a gene encoding ADP glucose pyrophosphorylase. No guidance has been presented for the identification or isolation of other genes involved in glycolysis. It is unclear whether plant transformation with genes encoding other glycolytic enzymes would alter glycolysis and/or kill the transformed plant cells and plants (see, e. g., page 3 of the specification, first full paragraph; page 3 of the ap Rees declaration filed 22 January 1993 in parent application Serial No. 07/991,451). It is also unclear whether plants transformed with more than one glycolytic gene would be adversely affected, given the "double dose" of glycolytic enzyme alteration.

Furthermore, von Schaewen et al. demonstrate the unpredictability inherent in the transformation of plants with genes encoding glycolytic enzymes. The transformation of tobacco resulted in dwarfing, bleaching and browning of leaves, and root stunting (see, e. g., page 3037). The lack of such deleterious effects on plant health in the potato plants transformed with the PFK gene has been previously argued by Applicants as evidence of unexpected results. Respiration, i. e. glycolysis, was also inhibited (see, e. g., page 3039, column 1, bottom paragraph).

Furthermore, the transformation of a different plant species by von Schaewen et al. resulted in a completely different response to the introduction of a glycolytic gene, i. e. lack of appreciable change in phenotype or starch content (see, e. g., page 3038, column 1, top paragraph; page 3039, column 2, bottom paragraph).

Thus, undue experimentation would be required by one of ordinary skill in the art to identify and isolate the gene or genes which encode any other glycolytic enzyme, and to evaluate the effects of said gene(s) on transformed plant cells and plants, given the unpredictability inherent in the process as discussed supra, and given the lack of guidance regarding the identification, isolation and characterization of the gene(s) encoding any other glycolytic enzyme.

Furthermore, ap-Rees et al. teach that only three out of many glycolytic or starch metabolic enzymes are cold-labile in potato (see, e.g., paragraph bridging pages 377 and 378; page 384; pages 390-391). Thus, transformation with genes encoding cold-tolerant enzymes would not affect the accumulation of sucrose in cold storage. Therefore, claim 19 should be limited to the exemplified phosphofructokinase gene, given the lack of guidance in the specification regarding the identification or isolation of other genes, the unpredictability inherent in the survival and health of plants transformed with a variety of

glycolytic genes as discussed supra, and the limited cold sensitivity of the enzymes as discussed supra.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 7, 10-12 and 17-18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Grill et al. (WO 89/08145). Grill et al. teach potato transformation with a viral vector containing a chimeric gene comprising a viral coat protein promoter and a bacterial cyclodextrin glucotransferase gene which encodes two forms of a starch degrading enzyme (see, e. g., pages 37-39; pages 49-51).

Claim 18 is rejected under 35 U.S.C. § 102(b) as being anticipated by Gay et al. Gay et al. teach the cloning of a bacterial levansucrase gene, and the expression of this gene in a heterologous host under the control of a promoter (see, e. g., page 1427, column 1, first full paragraph; page 1428, column 2, second paragraph). The ability of the coding sequence to be expressed in the cells of a plant would have been an inherent property.

Claim 18 is rejected under 35 U.S.C. § 102(b) as being anticipated by Khursheed et al. Khursheed et al. teach a chimeric gene comprising a promoter which functions in plants and

the α-amylase gene which encodes a starch degrading enzyme, and also teaches a plasmid containing the gene (see, e. g., page 18954, column 1, third full paragraph; page 18956; page 18957, column 1, Figure 4).

Claim 18 is rejected under 35 U.S.C. § 102(b) as being anticipated by Hellinga et al. Hellinga et al. teach a chimeric gene encoding bacterial phosphofructokinase under the control of a strong promoter, wherein said chimeric gene is contained in a plasmid (see, e. g., page 365, column 2, second full paragraph; pages 366-367). The ability of the coding sequence to be expressed in a plant would have been an inherent property.

Claims 9-11 and 18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Leung et al. Leung et al. teach a plasmid vector comprising a DNA fragment which comprises a chimeric gene comprising a bacterial ADPGPP (glgC) gene and a bacterial glgB (branching enzyme) gene, wherein the plasmid was transferred to another bacterium and resulted in the expression of the genes (see, e.g., page 82, column 2; page 83, column 1, top two paragraphs, column 2, bottom paragraph; page 84). Thus, the DNA fragment inherently contained the promoters associated with the structural genes. The ability of the coding sequence to be expressed in a plant would have been an inherent property.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section

102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim 8 is rejected under 35 U.S.C. § 103 as being unpatentable over Grill et al. (WO 89/08145). Grill et al. teach potato transformation with a viral vector containing a chimeric gene comprising a viral coat protein promoter and a bacterial cyclodextrin glucotransferase gene which encodes two forms of a starch degrading enzyme as discussed supra, but do not teach the transformation of a particular potato cultivar. It would have been obvious to one of ordinary skill in the art to utilize the method of potato transformation taught by Grill et al., and to modify that method by incorporating any known potato variety, given the recognition by those of ordinary skill in the art that choice of potato variety to be transformed would have been the

optimization of process parameters. Thus, the claimed invention was clearly prima facie obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Claims 1 and 17 are rejected under 35 U.S.C. § 103 as being unpatentable over Houck et al. (WO 88/09334) taken with Gay et al. Houck et al. teach the obtention of a tomato fruit-specific promoter and plant transformation with a chimeric gene comprising the promoter and a structural gene (see, e. g., paragraph bridging pages 11 and 12; pages 24-26; page 29). Houck et al. also suggest the use of the fruit-specific promoter for the expression of a heterologous sugar degrading enzyme, such as levansucrase, for varying the fruit phenotype (see, e. g., page 6, lines 25-31). Houck et al. do not teach plant transformation with a plant expressible promoter and a gene encoding sugar degradation. Gay et al. teach the cloning of a bacterial levansucrase gene, and the expression of this gene in a heterologous host (see, e. g., page 1427, column 1, first full paragraph; page 1428, column 2, second paragraph). Gay et al. also teach the probable existence of an alternative form of the enzyme before cleavage of a signal peptide (see, e. g., page 1429, column 2, first full paragraph). It would have been obvious to one of ordinary skill in the art to utilize the method of tomato transformation with a fruit-specific promoter and structural gene as taught by Houck et al., and to modify that

method by incorporating the levansucrase gene taught by Gay et al., given the suggestion to do so by Houck et al. and the recognition by those of ordinary skill in the art that each would have continued to function in its known and expected manner. Thus, the claimed invention was clearly prima facie obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Claims 1-4, 7-19 and 21-24 are rejected under 35 U.S.C. § 103 as being unpatentable over Twell et al. taken with de Graaff et al., Ap-Rees et al. and Yang et al. Twell et al. teach the transformation of potato with the tuber-specific patatin promoter and a heterologous structural gene, wherein said transformation resulted in the obtention of whole transformed plants and tubers (see, e. g., page 371). Twell et al. also suggest the use of the patatin promoter for tissue specific expression of a variety of heterologous structural genes (see, e.g., page 366, column 1, second full paragraph). Twell et al. do not teach potato transformation with the pyruvate kinase gene. De Graaff et al. teach the cloning of a fungal pyruvate kinase gene and its expression in a heterologous host, and also teach this enzyme's structural and functional similarities between various divergent hosts, as well as the conservation of the corresponding gene (see, e. g., paragraph bridging pages 315 and 316; page 316, column 1, penultimate paragraph; page 317; page 319, column 1). Ap-Rees et al. teach the relationship between

sucrose accumulation in cold-stored potato and loss of activity of a few enzymes including pyruvate kinase, and also teach the undesirability of sucrose accumulation in stored potatoes (see, e.g., pages 377-378; page 384; pages 390-391). Yang et al. teach the use of transformation to alter potato tuber quality, and suggest the use of the patatin promoter (see, e. g., page 99, paragraph bridging columns 1 and 2; paragraph bridging pages 109 and 110; page 110, first full paragraph). It would have been obvious to one of ordinary skill in the art to utilize the method of potato transformation taught by Twell et al., and to modify that method by incorporating the pyruvate kinase structural gene taught by de Graaff et al.; given the teaching by Ap-Rees et al. of the relationship between tuber sweetening and pyruvate kinase activity, the suggestion by Yang et al. to utilize plant transformation for potato tuber quality improvement, and the recognition by those of ordinary skill in the art that each would have continued to function in its known and expected manner. Thus, the claimed invention was clearly prima facie obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Claims 20 and 25-26 are deemed free of the prior art, in view of the unpredictability inherent in the expression of glycolytic genes in whole plants as discussed supra, and in view of the demonstration by Applicants that the transformation of potato plants with the exemplified phosphofructokinase or ADPGPP

genes exhibited desirable levels of starch accumulation without deleterious effects on plant health, as stated in allowed parent application Serial No. 07/991,451.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

April 27, 1995

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180